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American Society of Anesthesiologists

Volume 86 ■ Number 8 ■ August 2022
asamonitor.org

ASA Monitor®

THE LEADING SOURCE FOR PERIOPERATIVE HEALTH CARE NEWS

Who Is Immunocompromised?

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Editor-in-Chief

Immunocompromised patients are at increased risk of severe illness, hospitalization, and death from COVID-19 compared to immunocompetent patients (*Infect Dis Clin North Am* 2022;36:397-421). A decade or so ago, it was common to think of immunosuppression as an uncommon condition, applying to patients with HIV, some cancer patients on chemotherapy, transplant recipients, or patients with rare genetic disorders. That is no longer the case. Immunosuppression is now common in the treatment of inflammatory and autoimmune disorders. Corticosteroids are the classical immunosuppressants.

The contemporary list of immunosuppressants includes:

- TNF inhibitors (adalimumab, certolizumab, etanercept, golimumab, and infliximab)
- Interleukin inhibitors (anakinra, ustekinumab, secukinumab, sarilumab, siltuximab, sulfasalazine, tildrakizumab, tocilizumab, chloroquine, and hydroxychloroquine)
- Janus kinase (JAK) inhibitors (baricitinib, filgotinib, and tofacitinib)
- Calcineurin inhibitors (cyclosporine and tacrolimus)
- Metabolic inhibitors (azathioprine, leflunomide, mercaptopurine, methotrexate)
- mTOR (mammalian target of rapamycin) inhibitors (sirolimus [rapamycin], everolimus, and zotarolimus)
- Inosine monophosphate dehydrogenase inhibitors (mycophenolate)
- Phosphodiesterase inhibitors (apremilast)
- B cell inhibitors (rituximab)
- T cell inhibitors (abatacept)

This incomplete list highlights the advances in targeted immunotherapy. That young, vibrant, healthy colleague sitting

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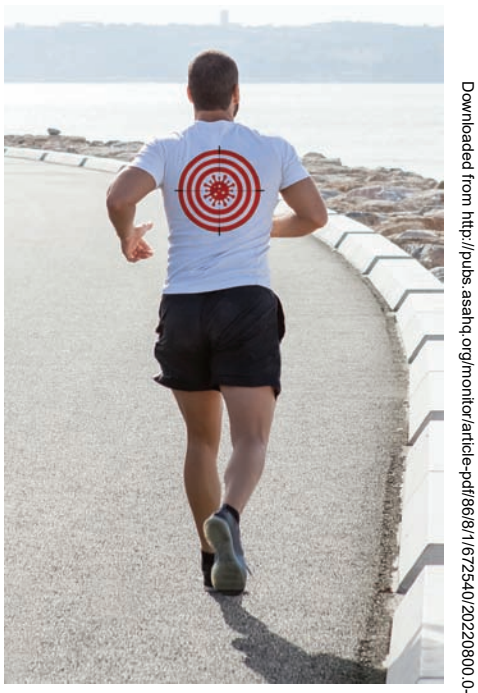

Your Hospital Put Out an RFP – What Do You Do Now?

Jason Greenberg, MD Joseph Szokol, MD, MBA, FASA
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Consider this (not uncommon) scenario: Sleepy Anesthesia Group (SAG) has been providing exclusive services at Hospital XYZ for over 15 years, and suddenly they learn that the hospital has put out a request for proposal (RFP) for anesthesia services. SAG feels caught off guard – what should they do?

Find the trigger: The first step is to assess why the hospital published an RFP. What triggered this? Possibilities include:

1. The hospital may have requested services (more OR coverage, additional non-operating room locations, a perioperative surgical home [PSH], a more robust quality program, or other service enhancements) that the group has been slow, or unwilling, to provide.

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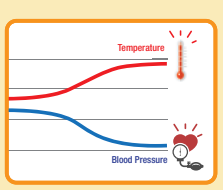

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Guest Editors: Uday Jain, BSEE, MD, PhD, FASA, and Kumar G. Belani, MBBS, MS, FACA, FAAP, SAMBA-F

How Motown's 'Last Dollar Choice' Philosophy Inspired ASA's Early Career Membership Program

Kenneth Moran, MD, FASA George Williams, MD, FASA, FCCM, FCCP

At the height of Motown Records' success, leaders of the organization employed something they called the "Last Dollar Choice." With each potential record, they'd ask themselves if a customer with a single dollar to spend would consider the music to be more valuable than a sandwich. If the answer was no, the record didn't make the cut. If it was yes, it did.

Value was a touchstone in Detroit during Motown's heyday, just as it's a touchstone for ASA today. Every member should expect to get real value for their membership, but not all members share the same needs. In the decades to come, today's early-career physicians will shape the specialty and ASA. While it's essential to engage young anesthesiologists in their first few years of practice, it is equally important to recognize that they view the idea of society membership through a unique lens with specific priorities, needs, and expectations. It's a suite of concerns ASA has committed to understand and address so we can deliver genuine value, advance the practice, and secure our future.

Like the leaders of Motown, the Committee on Membership wanted to create so much value that young anesthesiologists wouldn't hesitate to join our ranks and would recognize the many benefits of ASA membership. Through surveys, studies, and interviews, we learned that financial pressures, work-life balance demands, exam concerns, and even a different relationship to technology were drivers for anesthesiologists in the first few years of practice. In developing the

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In the Know: Immunocompromised

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next to you in a cafeteria or conference room may be immunosuppressed and at risk of severe illness or death from COVID-19.

A 2016 report reviewed the 2013 National Health Interview Survey of 34,426 adults (*JAMA* 2016;316:2547-8). The survey asked participants whether a "doctor or other health professional" told them they had a weakened immune system. Those answering "yes" were asked more detailed questions. Four percent of the respondents had been told they had weakened immune suppression, and of these, roughly two-thirds (2.8%) also had additional evidence of immunosuppression.

Two-thirds of immunosuppressed respondents were women. The highest estimated U.S. prevalence was in adults 50-59 years of age (4.4%), followed by 60-69 years of age (3.9%), and 70-79 years of age (3.1%). The authors suggested the higher levels of immunosuppression in women might be a result of women being at higher risk for autoimmune disorders.

A 2021 JAMA report estimated the prevalence of immunosuppressive therapy among U.S.-based adults for the years 2018-2019 in a national insurance claims database (*JAMA Netw Open* 2021;4:e214920). Drug-induced immunosuppression was defined as:

1. One or more doses of an antineoplastic immunosuppressant
2. Oral glucocorticoid therapy for 30 days or more
3. Oral or subcutaneous immunosuppressive therapy for 90 days
4. Two or more doses of intravenous noncorticosteroid immunosuppressant.

Among the more than 3 million patients in the study, 2.8% met the criteria for drug-induced immunosuppression. The most frequent immunosuppressive drugs were oral corticosteroids (67.7%), disease-modifying antirheumatic drugs and anti-rejection therapies in transplant patients (25.9%), methotrexate (24.5%), and TNF inhibitors (22.7%). The most frequent diagnoses associated with immunosuppression were neoplasm (73.8%), immune-mediated conditions (68.8%), and inflammatory skin conditions (38.8%).

Consistent with the 2016 report, about 60% of the immunosuppressed individuals were women. The largest number of patients were aged 56-64 years.

Immunosuppression and COVID-19

Immunosuppression increases the risk of serious illness and dying from COVID-19. In a study of patients with rheumatic diseases, rituximab, sulfasalazine, azathioprine, cyclophosphamide, cyclosporin, mycophenolate, or tacrolimus, but not methotrexate, were associated with an increased risk of death (*Ann Rheum Dis* 2021;80:930-42). In patients with irritable bowel disease, corticosteroids are associated with increased risk of severe disease, but not TNF antagonists and methotrexate (*Gastroenterology* 2022;162:316-319.e5).

Severe clinical outcomes are common in patients with HIV, particularly those with lower CD4 cell counts (*Clin Infect Dis* 2021;73:e1964-e1972; *Lancet HIV* 2021;8:e701-e710). Severe clinical outcomes including death are also more common in patients with kidney transplants and liver transplants (*N Engl J Med* 2020;382:2475-7; *Transplant Direct* 2022;8:e1292; *Sci Rep* 2022;12:4831). The infection fatality rate for patients with secondary immunodeficiency syndrome is about 50% higher than for the general population (*Clin Exp Immunol* 2022:uxac008). The infection fatality rate for patients with interferon antibodies is more than twice as high as the general population (*Proc Natl Acad Sci U S A* 2022;119:e2200413119).

Immunosuppression and vaccination

In a report published in the Morbidity and Mortality Weekly Report in 2021, which was subsequently published in the *American Journal of Transplantation*, researchers from the CDC compared the effectiveness of two doses of the mRNA vaccines (Pfizer and Moderna) in 21,101 immunocompromised patients with 69,116 matched immunocompetent adults. Half of the patients were considered "fully vaccinated" by CDC guidelines (*MMWR Morb Mortal Wkly Rep* 2021 Nov 5;70:1553-9; *Am J Transplant* 2022;22:306-14). The vaccine efficacy for COVID-19-associated hospitalization was lower for the immunocompromised adults (77%) than for the immunocompetent adults (90%). Among immunocompromised adults, vaccine efficacy was lowest in organ or stem cell transplant recipients (59%) and the highest in patients with rheumatologic or inflammatory disorders (81%). The studies formed the basis of CDC guidelines recommending that immunocompromised adults receive three mRNA vaccines followed by a booster six months after the third dose (asamonitor.pub/3OpWkVb).

Immunosuppression and the pandemic

In February, The Atlantic published an excellent article that discussed how the pandemic has not ended for the immunosuppressed (*The Atlantic* February 2022). As the authors note, "Over the past year, as many Americans reveled in their restored freedoms, many immunocompromised people felt theirs shrinking." We have personally had otherwise healthy immunosuppressed friends and colleagues become incredibly ill from Omicron BA.2.

Several strains have emerged during the pandemic with a constellation of new mutations that escape existing immunity and increase infectiousness, the most recent being Omicron. There is considerable evidence that these highly adapted multi-mutational strains evolved in immunocompromised individuals (*Science* 2022;375:1122-7; *N Engl J Med* 2022;386:1867-8).

We chose to write this story after attending a recent medical meeting, where a colleague from another institution asked why our contingent was still wearing masks. "Don't you know the pandemic is over?" Our answer was, "No, it isn't. One of us is severely immune suppressed." The colleague responded, sheepishly, "Oops, I had no idea."

Immunosuppression is widely used in medicine. You can't tell who is immunosuppressed. As a result, our safest approach to patients, colleagues, friends, and family may be to maintain non-pharmaceutical interventions (masks, social distancing, and avoiding indoor spaces) and aggressively self-test until we can be confident that we will not accidentally spread COVID-19 to those still at risk. ■